REMARKS

Claim 10, 14, 15, 32 and 36-38 are pending in the application. Claims 1-9, 11-13, 16-31, 33-35, 39-41 and 52-54 have been withdrawn. Claims 42-51 have been canceled previously

The Examiner first mentioned that the application contains claims directed to two distinct species: a soluble p97 and an antibody directed to p97. During a phone conversation with the agent on record, on October 2, 2007, a provisional election was made to prosecute the species of soluble p97. The Examiner requested affirmation of this election in replying to the pending Office Action. In this regard, the Applicants reaffirm that the species of soluble p97 is elected without traverse and that claims 11-13 are withdrawn. Reconsideration and withdrawal of the Examiner's rejection are earnestly solicited.

Specification

The Applicants wish to point out that the section "Brief description of the drawings" in the specification has been amended as submitted hereinabove in order to identify all sections of Figs. 15, 16, 19, 23, 24, 26 and 27 as requested by the Examiner.

Claim objection

The Applicants point out that the typographical error identified by the Examiner in claim 10 has been corrected.

Claim rejection - 35 USC § 112

Claims 36-38 have been rejected under 35 USC § 112, first paragraph. The Examiner mentions that, while the specification being enabling for a method for treating cancer caused by cells expressing melanotransferrin (p97), does not reasonably provide enablement for a method treating just any cancer. The Examiner further points out that the specification discloses that exogenous p97 inhibits cell-migration of HMEC-1 and SK-MEL28 cell lines. The Examiner also recognizes that the specification also discloses that soluble p97 inhibits angiogenesis in HMEC-1

and HUVEC cell lines. However, the Examiner is of the opinion that those of skill in the art recognize that *in vitro* assays and/or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drug. However, clinical correlations are generally lacking. Thus, the Examiner is of the opinion that due to the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated.

Firstly, the applicants wish to respectfully submit that the anti-tumoral and anti-angiogenic effect of soluble p97 is not restricted to or specific to cells expressing p97 or MTf. Enclosed herewith is a Declaration b Dr. Michel Demeule demonstrating that sMTf treatment decreases the angiogenesis stimulated by growth factors and leads to efficient growth inhibition of subcutaneous U-87 MG and NCI-H460 cells. Consequently, since U-87 cells do not express mMTf, it is thus concluded that sMTf treatment exerts anti-angiogenic and anti-tumor activities not only-in a MTF-expressing environment, but also on cells not expressing mMTf.

Further, it is also demonstrated in the Declaration that sMTf treatment clearly decreases tumor development *in vivo*. Constant delivery of sMTf into nude mice with Alzet micro-osmotic pumps contributed to a significant reduction in the growth of subcutaneous U-87 MG-derived tumor. Thus, the Applicants have disclosed and exemplified the utility of the present invention *in vitro* and *in vivo*. The Applicants believe that in order to convince the Examiner of the enablement of the present invention, as per her requirement, clinical trials would have been initiated before this application would have been filed. Requesting clinical trial results to demonstrate enablement of the present invention is unreasonable and represents an undue burden, burden that does not exist in any other field of invention. Applicants respectfully submit that it is stated in the Manual of Patent Examining Procedure (MPEP 2107.03, section IV) that "*Office personnel should not impost on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders.*

The Applicants wish to submit that, only when the pre-clinical data is promising, a company makes a decision on whether to begin the long and costly process of clinical trials. Most companies file for and receive patents for the commercial uses of the compound that they are developing during pre-clinical trials to not only protect their invention, but also to reassure investors that the invention which will be undergoing clinical phase trials is patented. Assuming the company decides to pursue human studies, it must first submit an Investigational New Drug (IND) application to the FDA for approval. The IND must provide pre-clinical data of sufficient quality to justify the testing of the drug in humans. It is believed that in order for the present invention to be commercially and financially viable, Applicants need to protect their invention first by filing a patent application before submitting an IND application to the FDA. The Applicants believe that the Examiner is not examining the present application in terms of its patentability, but in terms of its liability to pursue human studies, which is believed to be the role of the FDA and not of the USPTO. Consequently, applicants feel that, in view of the arguments presented by the Examiner, it is easier to obtain an FDA approval to start clinical phase trials than meeting the criteria of patentability imposed by the Examiner. The applicants wish to also submit that the Examiner specifically points out on page 9 of the pending Office Action that "*since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only **39** that are used exclusively for chemotherapy, as opposed to supportive care, have shown approval from the FDA*". The position of the Examiner is contradictory to what the scientific community and the FDA adopts as a normal way to proceed since testing in animal and *in vitro* models are necessary to apply for an IND. The pre-clinical data of sufficient quality are absolutely requested to justify the testing of the drug in humans. 39 success stories, as acknowledged by the Examiner, are believe to be a convincing number to support the ability of *in vitro* and *in vivo* models to predict the efficacy of compounds in human.

In view of the Declaration submitted herewith and the arguments presented hereinabove, reconsideration and withdrawal of the Examiner's rejection are earnestly solicited.

Claim rejections - 35 USC § 102

Claims 10, 14, 32, 36-38 have been rejected under 35 USC § 102(b) as being anticipated by the reference of Gabathuler et al. The Examiner is of the opinion that the mentioned reference teaches a pharmaceutical composition comprising soluble p97 conjugated to a chemotherapeutic agent for treating brain tumors. In this regard, the Applicants wish to submit that the reference of Gabathuler et al. relates to drug delivery compositions for enhanced delivery of chemotherapeutic agents to tumors in or around the brain, for reducing the systemic toxicity of chemotherapeutic agents used in treating tumors in and around the brain. This reference teaches that chemotherapeutic agents, which are linked to p97, thus forming a p97-chemotherapeutic agent complex, are excellent vehicles for enhanced delivery of chemotherapeutic agents to brain tumors and other neoplasia located on or around the brain and for improved treatment of such tumors and neoplasia. As clearly stated on page 1, paragraph [0008] in Gabathuler et al., the invention disclosed in the mentioned reference "*demonstrates that chemotherapeutic agents which are lined to p97, thus forming a p97-chemotherapeutic agent composition, are excellent vehicles for enhanced delivery of the chemotherapeutic agents to brain tumors*". Nowhere is there any teaching or suggestion in Gabathuler et al. that soluble p97 alone can regulate the activation of plasminogen, cell migration or angiogenesis. On the contrary, the reference of Gabathuler et al. as a whole only teaches that the p97 is a transporter of chemotherapeutic agents to the brain (see paragraph [0002] describing the purpose of the invention). Further, this enhanced delivery is only demonstrated for brain tumors and not other types of cancer. There is no teaching or suggestion in Gabathuler et al. of using non-conjugated soluble p97 for treating cancer. Gabathuler always uses the p97 conjugated to a chemotherapeutic agent for delivery of said agent. Furthermore, Gabathuler defines the chemotherapeutic agent at paragraphs [0009] and [0029]. It is clear from paragraph [0029] that Gabathuler never contemplated p97 alone or in itself as a chemotherapeutic agent for treating cancer. Thus, it is believed that the reference of Gabathuler et al. does not anticipate claims 10, 14, 32, 36-38 and reconsideration and withdrawal of the Examiner's rejection are earnestly solicited.

Conclusion

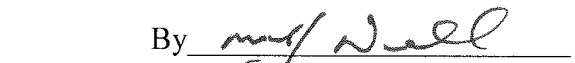
In view of the above remarks, it is believed that claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: April 17, 2008

Respectfully submitted,

By 

Mark J. Nuell
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
12770 High Bluff Drive
Suite 260
San Diego, California 92130
(858) 792-8855
Attorney for Applicant